Remarks

Claims 38, 41, 42, 45, 46, 48, and 49 are pending in the application. Claims 38, 41, 42, 45, 46, 48, and 49 have been amended; and claims 39, 40, 43, 44, and 47 have been canceled. No new matter has been added. Applicants believe these amendments and cancellations serve a useful clarification purpose, and are desirable for clarification purposes, independent of patentability. Accordingly, Applicants respectfully submit that the claim amendments and cancellations do not limit the range of any permissible equivalents.

Objection to the Specification

The Examiner objected to the specification, correctly noting that the cited reference of Slifman et al. did not purify MBP. In response, Applicants have corrected the specification to clarify that Slifman isolated EDN and ECP and Applicants used this Slifman technique to isolate MBP.

35 U.S.C. §112 Rejections

At the outset, Applicants note that as stated by the Examiner, the level of skill in this field of study is extremely high. Skilled artisans in the relevant field, which in this case may include medical researchers with one or more advanced degrees, several years of experience in drug development and research, and perhaps assistants and other resources normally available in the research and development of therapeutic agents, would understand from the disclosure in this application that the Applicants were in possession of the invention. Simply put, the issues raised to challenge the claims – namely that Applicants did not specify a set amount of MBP to be given to a subject of a given weight – ignores the fact that these issues would be readily understood by skilled artisans.

Compliance with the written description and enablement standards does not require an applicant to provide information that would be potentially trivial to a person of ordinary skill in the art or possibly require routine research. Applicants respectfully submits that doctors, medical researchers, and other persons of ordinary skill in the field having the benefit of this disclosure

would not only recognize that Applicants had possession of the invention, but also would understand how to use the disclosure.

Enablement

Claims 42-45 were rejected under 35 U.S.C. §112, first paragraph as not being enabled. Points 10, 15, 16, 18, and 19 relate to the enablement rejection. For the reasons set forth below, Applicant respectfully disagrees with this rejection and submits that claims 42-45 are enabled by the specification.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation. *United States v. Telectronics, Inc.*, 857 F.2d 778, 784, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988), MPEP § 2164.01. A patent need not teach, and preferably omits what is well known in the art. *In re Buchner*, 929 F.2d 600, 661, 18 USPQ2d 1331, 1332 (Fed. Cir 1991), MPEP § 2164.01. The fact the experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriesr*, 221, USPQ 1165, 1174 (Int'l Trade Comm'n 1983), MPEP § 2164.01. For example, it is not necessary to specify the dosage or method of use if it is known to one skilled in the art that such information could be obtained without undue experimentation. MPEP § 2164.01(c).

Point 10 of the Office Action asserts that undue experimentation would be needed to determine how to administer "cytotoxic proteins to a subject which will not elicit an inflammatory immune system response while still functioning to inhibit heparanase glycosidase activity." Each of the pending claims recites MBP. There are no reports to date that MBP may be toxic, except for only one report, where MBP was administered directly to guinea pig bronchi. However, damage to the epithelial tissue was only observed when MBP was delivered at very high concentrations, at 10^{-4}M (Tagari et al., Agents Actions, vol. 37, pp.171-3, 1992). A copy of the abstract of this article is enclosed. This concentration is about between 100-1,000 times higher than the dosages used in the present study. Moreover, specific toxicity tests should be recommended by the physician in charge of the patient. It is a well known fact that a vast

number of anti-cancer treatments are highly toxic, even at therapeutic dosages. Thus, Applicants respectfully submit that claims 42-45 are enabled, particularly since the Examiner concedes that the "relative skill of those in the art is exceedingly high" and the "predictability of whether the administration of the composition will adversely affect the subjects dues to an inflammatory immune response is huge."

Point 19 of the Office Action seems to indicate that unpublished inventors' data (relating to Example 3 of the specification and noted in the Response filed March 9, 2005) showing that the mice treated with MBP were viable and had no adverse or negative immune response would be considered once made of record. Applicants submit that by making the statement in the prior Response, it is of record. Nevertheless, Applicants can submit a declaration presenting the non-published data if the Examiner deems this necessary.

Applicants have amended claim 42 as required by the Examiner to address Point 15 of the Office Action.

Point 16 of the Office Action asserts that undue experimentation would be needed to determine the dosage needed to inhibit heparanase glycosidase activity in subjects of varying weight. Claim 42 now recites the step of administering a therapeutically effective amount of an eosinophil secondary granules basic protein which is the 117 amino acid residue of MBP (Major Basic Protein) in a concentration of from about 1 to about 180 μg/ml.

The phrase "effective amount" is used throughout the specification and is defined in the specification as "an amount necessary to achieve a selected result. For example, an effective amount of the composition of the invention useful for inhibition of heparanase activity and thereby for the treatment of said pathology." See e.g. ¶ [0135]. Applicants respectfully submit that it is not necessary to provide an absolute amount in order to satisfy the enablement requirement. Patent applications are not required to be cookbooks reciting every step, measurement, or aspect of an invention. In this case, such information is known or readily available to those of ordinary skill in the art. In addition, similar claim language may be found in the claims of a number of issued patents.

In light of the foregoing, Applicants submit that claims 42-45 are enabled by the specification. Accordingly, Applicants respectfully request reconsideration and withdrawal of

the 35 U.S.C. 112 rejection.

Written Description

Claims 46-49 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Points 11 and 18 of the Office Action relate to the written description rejection. For the reasons set forth below, Applicants respectfully disagree and submit that the subject matter of claims 46-49 is fully supported by the specification.

With respect to Point 11, the claims have been amended in an effort to expedite prosecution and without admitting the validity of the rejection. In particular, the independent claims now recite eosinophil secondary granules basic protein which is the 117 amino acid residue of MBP (Major Basic Protein). The scope of claims 41, 45 and 48 has also been amended accordingly, while other claims which have become redundant have been cancelled.

Applicants also submit that the claim amendments address Point 18 of the Office Action. However, with respect to the statements made regarding the pharmaceutically acceptable carrier, Applicants note that the specification indicates that control cells were treated with saline (see Example 5) and one of ordinary skill in the art would understand that MBP was likewise diluted in saline or an analogous carrier so that the control served its intended function.

In light of the foregoing, reconsideration and withdrawal of the written description requirement rejection is respectfully requested.

35 U.S.C. §102(a) Rejection

Claims 38-41 were rejected under 35 U.S.C. 102(a) are being anticipated by Davis et al. In an effort to expedite prosecution and without admitting the validity of this rejection, claim 38 now recites that the second constituent is an eosinophil secondary granules basic protein which is the 117 amino acid residue of MBP (Major Basic Protein). Accordingly, Applicants respectfully submit that claim 38 (and dependent claim 41) is not anticipated by Davis et al.

Conclusion

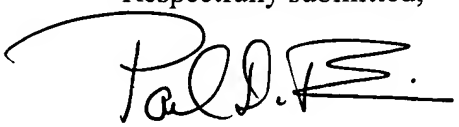
For all of the above reasons, the claim rejections are believed to have been overcome,

placing claims 38, 41, 42, 45, 46, 48, and 49 in condition for allowance, and reconsideration and allowance thereof is respectfully requested.

The Examiner is encouraged to telephone the undersigned to discuss any matter that would expedite allowance of the present application.

Fees for a six (6) month extension of time and a Request for Continued Examination (RCE) are believed to be due and are submitted via Credit Card Payment Form. However, please charge any required fee (or credit any overpayments of fees) to the Deposit Account of the undersigned, Account No. 500601 (Docket No. 7640-X04-017).

Respectfully submitted,



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1: Agents Actions. 1992 Nov;37(3-4):171-3. Related Articles, Links

Quantitation of eosinophil Major Basic Protein cytotoxicity to rodent respiratory epithelium.

Tagari P, Chee P, Chan C, McKee K, Black C, Nicholson D, Ford-Hutchinson AW.

Department of Pharmacology, Merck Frosst Institute for Therapeutic Research, Pointe Claire-Dorval, Quebec, Canada.

Eosinophil Major Basic Protein (MBP) may be a potent effector in damaging airway epithelium and inducing acute (2-3 h) hyperresponsiveness to agonists in primates. Accordingly, interactions between human eosinophil MBP and guinea-pig airway epithelium were quantitated biochemically. MBP was extracted from human eosinophils and purified by size-exclusion HPLC. This resulted in a single protein band on electrophoresis, which cross-reacted with antisera raised to peptides derived from the predicted sequence of human MBP. This human MBP caused modest, but statistically significant, damage to respiratory epithelium (16.4% increase in efflux of 51Cr from guinea-pig tracheal rings) after 3 h of incubation with 10(-4) M concentration, but not with lower concentrations. These data demonstrates that MBP cytotoxicity to intact epithelium can be rapidly measured in vitro, and suggests that rodent airway epithelium may be relatively resistant to the cytotoxic effects of MBP.

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